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(54) USE OF SALICYLIC ACID FOR REGULATING SKIN ATROPHY

VERWENDUNGVON SALICYLSÄURE ZUR KONTROLLE DER HAUTATROPHIE

EMPLOI D'ACIDE SALICYLIQUE CONTRE L'ATROPHIE CUTANEE

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Description

[0001] The present invention relates to the field of anti-aging of skin. Specifically, the invention relates to novel cosmetic methods for regulating atrophy in mammalian skin.

[0002] Skin is subject to abuse by many extrinsic (environmental) factors as well as intrinsic (chronoaging) factors. A common extrinsic factor is exposure to ultraviolet radiation. Whether extrinsic or intrinsic, the abuse results in wrinkling of the skin. To many people, skin wrinkles are a reminder of the disappearance cf youth. As a result, the elimination of wrinkles has become a booming business in youth-conscious societies. Treatments range frog cosmetic creams and moisturizers to various forms of cosmetic surgery.

[0003] Chronoaging results in the thinning and general degradation of skin. As the skin naturally ages, there is a reduction in the cells and blood vessels that supply the skin. There is also a flattening of the dermal-epidermal junction which results in weaker mechanical resistance of this junction. As a consequence, older persons are more susceptive to blister formation in cases of mechanical trauma or disease processes. (See Oikarinen, (1990) "The Aging of Skin: Chronoaging Versus Photoaging", Photodermatal, Photoimmunol., Photomed., Vol. 7, pp 3-4).

[0004] It is known to use salicylic acid for the treatment of acne, see for example, US-A-4,891,227 and US-A-4,891,228, to Thaman et al., both issued January 2, 1990. Further, salicylic acid has been used for the removal of wart, corns and calluses; for the treatment of psoriasis, seborrheic dermatitis and dandruff; and for the topical treatment of ringworm infection. US-A-4,608,370 discloses a skin treatment composition comprising 3-7 parts salicylic acid 8-12 parts resorcinol, 8-12 parts lactic acid and 60-90 parts ethyl alcohol for light peeling of dead surface skin and removal of blemishes. EP-A-0 434 628 discloses compositions for anti-ageing or acne comprising vitamin A ester and salicylic acid. Japanese Patents Gazette, week 8322, Derwent Publications Ltd., London, GB discloses a cosmetic pack for prevention and recovery of wrinkles containing salicylic acid and a substrate. US-A-3 821 370 discloses a skin composition comprising phenol salt, a salicylate, resorcinol and a zinc compound for minimizing the appearance of surface blemishes. US-A-5 017 367 discloses compositions for cleaning, moisturising and healing of skin irritations where salicylic acid can be used as a preservative. EP-A-0 378 936 discloses a composition for treating ageing skin comprising a salicylic acid derivative and optionally retinoic acid derivatives. A listing of commercially available products containing salicylic acid will be found in the Physician's Desk Reference, 45th Edition, 1991, page 323. However, these prior art uses of salicylic acid have generally involved short term treatments in which relatively large doses of the acid are applied (i.e., sufficient to cause significant irritation and often peeling) in order to obtain a cure or treatment of the particular condition, such as removal of comedones, as opposed to persistent treatment of normal aging skin.

[0005] It is an object of the present invention to provide a cosmetic method of regulating atrophy in mammalian skin which comprises treating mammalian skin with a safe and effective amount of an anti-wrinkle/anti-atrophy agent excluding methods for treatment of the human or animal body by surgery or therapy or diagnostic methods.

[0006] According to a further aspect of the present invention there is provided the use of a safe and effective amount of salicylic acid and a pharmaceutically-acceptable hydroalcoholic carrier in a composition for treating the skin to regulate atrophy.

[0007] The present invention further relates to cosmetic methods for regulating atrophy in mammalian skin comprising chronic treatment of the skin with a safe and effective amount of salicylic acid.

[0008] All percentages and ratios used herein are by weight and all measurements are at 25°C unless otherwise indicated.

[0009] As used herein, "alkyl" means an unsubstituted carbon-containing chain which may be straight, branched or cyclic, preferably straight or branched, more preferably straight; saturated, monounsaturated (i.e., one double or triple bond in the chain), or polyunsaturated (i.e., two or more double bonds in the chain; two or more triple bonds in the chain; one or more double and one or more triple bonds in the chain), preferably saturated.

[0010] As used herein, "topical application" means directly laying on or spreading on outer skin.

[0011] As used herein, "pharmaceutically-acceptable" means that drugs, medicaments or inert ingredients which the term describes are suitable for use in contact with the tissues of humans and lower animals without undue toxicity, incompatibility, instability, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio.

[0012] As used herein, "skin atrophy" means the thinning and/or general degradation of the dermis often characterized by a decrease in collagen and/or elastin as well as decreased number, size and doubling potential of fibroblast cells. Skin atrophy is a natural result of aging. Skin atrophy is often an undesirable side effect resulting from treatment with corticosteroids.

[0013] As used herein, "regulating skin atrophy" means preventing, retarding, arresting, or reversing the process of atrophy in mammalian skin.

[0014] As used herein, "safe and effective amount" means an amount of compound or composition sufficient to significantly induce a positive modification in the condition to be treated, but low enough to avoid serious side effects (at a reasonable benefit/risk ratio), within the scope of sound medical judgment. The safe and effective amount of the compound or composition will vary with the particular condition being treated, the age and physical condition of the

patient being treated, the severity of the condition, the duration of the treatment, the nature of concurrent therapy, the specific compound or composition employed, the particular pharmaceutically-acceptable carrier utilized, and like factors within the knowledge and expertise of the attending physician.

[0015] As used herein, "chronic treatment" means continued treatment with an active agent over an extended period during a subject's lifetime, preferably for at least about three weeks, more preferably from about three months to about twenty years, more preferably from about six months to about ten years, more preferably still from about one year to about five years.

[0016] As used herein, all percentages are by weight unless otherwise specified.

Active Compound

[0017] The present invention relates to a cosmetic method for regulating atrophy in mammalian skin comprising treating the skin with a safe and effective amount of a composition comprising an salicylic acid active component excluding methods for treatment of the human or animal body by surgery or therapy or diagnostic methods. The salicylic acid active component can be used in combination with other active ingredients described below. The salicylic acid is used with a hydroalcoholic solution.

[0018] Salicylic acid is a well known active component and is generally described in US-A-4,514,385, to Damani, et al., assigned to Alcon Laboratories, issued April 30, 1985.

[0019] In the treatment herein the topical carrier comprises a hydroalcoholic solution at pH 2 to 4 of salicylic acid as the active anti-acne ingredient together with a specific anionic surfactant component. More preferably such active is a stable, hydroalcoholic composition having a pH value of from 2 to 4 and containing from 0.2 to 5.0 percent by weight of salicylic acid and from 0.2 to 5.0 percent by weight of sodium methyl cocoyl taurate and/or sodium methyl oleoyl taurate as the anionic surfactant component. Generally, a sufficient amount of a cosmetically acceptable alkaline component (i.e., alkalizing agent) to provide and maintain the composition with a pH from 2.0 to 4 is included.

[0020] As the alcohol component of the hydroalcoholic solvent, from 10 to 60 percent by weight of ethyl alcohol, measured as total C_2H_5OH content, is preferred although a like amount of isopropyl alcohol (C_3H_7OH) may also be beneficially utilized. From 30 to 80 percent by weight of water is also required as the aqueous component of the hydroalcoholic solvent.

[0021] The anionic surfactant component of this active composition, i.e., the taurate surfactant component, is specifically directed to sodium methyl cocoyl taurate and sodium methyl oleoyl taurate, both of which are readily available from diverse commercial suppliers, as noted in The Cosmetic, Toiletry and Fragrance Association (CTFA) Cosmetic Ingredient Dictionary, 3rd Edition, 1982, pages 286-287.

[0022] Although it is preferred to use the taurate surfactant as the sole surfactant in the active compositions, other surfactants may be included, the nonionic type having preference over the anionic type in view of the relative non-irritating characteristic to the skin of the former. Cationic type surfactants, which are most irritating to the skin, are less preferred because of their marked susceptibility to hydrolysis at the low acidic pH of the subject compositions.

[0023] The pH value of the preferred active component, from about 2 to about 3.5, may be achieved by use of appropriate cosmetically acceptable primary or dual buffer systems. In most instances, the resultant pH of the hydroalcoholic solution of salicylic acid is slightly below or at the lower end of the indicated range, and all that is required to adjust the pH to a desired higher value within the indicated range is to add an alkaline additive such as is commonly utilized in cosmetic formulations for such purpose. Although sodium carbonate is preferred, other suitable alkalizing agents include potassium carbonate, sodium hydroxide, potassium hydroxide, triethanolamine and the like. If deemed necessary to change or adjust the pH to a lower value, a suitable cosmetically acceptable acidifying agent such as citric acid may be employed.

Pharmaceutical Compositions

[0024] Treatment herein will employ the use of a topical pharmaceutical composition comprising the active compound and a pharmaceutically-acceptable carrier. The term "pharmaceutically-acceptable carrier", as used herein, means one or more compatible solid or liquid filler diluents or microencapsulating substances which are suitable for administration to a human or lower animal. Pharmaceutically-acceptable carriers must be of sufficiently high purity and sufficiently low toxicity to render them suitable for administration to the human or lower animal being treated. A safe and effective amount of carrier is from 50% to 99.99%, preferably from 99.9% to 80%, more preferably from 98% to 95%, of the composition.

[0025] Variations in formulation of these carriers will result in a wide variety of products which fall within the scope of the present invention.

[0026] The topical pharmaceutical compositions of the present invention may be made into a wide variety of product types. These include, but are not limited to solutions, lotions, creams, beach products, gels, sticks, sprays, pads;

ointments, pastes, mousses and cosmetics. These product types may comprise several types of carrier systems including, but not limited to solutions, emulsions, gels and solids.

[0027] The topical pharmaceutical compositions of the present invention formulated as solutions typically include a pharmaceutically-acceptable aqueous or organic solvent. The terms "pharmaceutically-acceptable aqueous solvent" and "pharmaceutically-acceptable organic solvent" refer to a solvent which is capable of having dispersed or dissolved therein the active compound, and possesses acceptable safety properties (e.g., irritation and sensitization characteristics). Water is a typical aqueous solvent. Examples of suitable organic solvents include: propylene glycol, butylene glycol, polyethylene glycol (200-600), polypropylene glycol (425-2025), glycerol, 1,2,4-butanetriol, sorbitol esters, 1,2,-6-hexanetriol, ethanol, isopropanol, butanediol, and mixtures thereof. Preferably, these solutions contain from 0.01% to 50% of the active compound, more preferably from 0.1% to 20%; and from 1% to 80% of an acceptable aqueous or organic solvent, more preferably from 1% to 40%.

[0028] If the topical pharmaceutical compositions of the present invention are formulated as an aerosol and applied to the skin as a spray-on, a propellant is added to a solution composition. A more complete disclosure of propellants useful herein can be found in Sagarin, Cosmetics Science and Technology, 2nd Edition, Vol. 2, pp. 443-465 (1972).

[0029] Topical pharmaceutical compositions of the present invention may be formulated as a solution comprising an emollient. An example of a composition formulated in this way would be a sunscreen-containing product. Preferably, such compositions contain from 0.1% to 50% of the active compound and from 2% to 50% of a topical pharmaceutically-acceptable emollient.

[0030] As used herein, "emollients" refer to materials used for the prevention or relief of dryness, as well as for the protection of the skin. A wide variety of suitable emollients are known and may be used herein. Sagarin, Cosmetics, Science and Technology, 2nd Edition, Vol. 1, pp. 32-43 (1972) contains numerous examples of suitable materials.

[0031] A lotion can be made from a solution carrier system. Lotions preferably comprise from 0.1% to 20%, more preferably from 1% to 5%, of the active compound; from 1% to 20%, preferably from 5% to 10%, of an emollient; and from 50% to 90%, preferably from 60% to 80%, water.

[0032] Another type of product that may be formulated from a solution carrier system is a cream. A cream of the present invention would preferably comprise from .1% to 20%, more preferably from 1% to 5%, of the active compound; from 5% to 50%, preferably from 10% to 20%, of an emollient, and from 45% to 85%, preferably from 50% to 75%, water.

[0033] Yet another type of product that may be formulated from a solution carrier system is an ointment. An ointment may comprise a simple base of animal or vegetable oils or semi-solid hydrocarbons (oleaginous). Ointments may also comprise absorption ointment bases which absorb water to form emulsions. Ointment carriers may also be water soluble. An ointment may also comprise from 2% to 10% of an emollient plus from 0.1% to 2% of a thickening agent. A more complete disclosure of thickening agents useful herein can be found in Segarin, Cosmetics. Science and Technology, 2nd Edition, Vol. 1, pp. 72-73 (1972).

[0034] If the carrier is formulated as an emulsion, from 1% to 10%, preferably from 2% to 5%, of the carrier system comprises an emulsifier. Emulsifiers may be nonionic, anionic or cationic. suitable emulsifiers are disclosed in, for example, US-A-3,755,560, issued August 28, 1973, Dickert et al; US-A-4,421,769, issued December 20, 1983, Dixon et al.: and McCutcheon's Detergents and Emulsifiers, North American Edition, pages 317-324 (1986). Preferred emulsifiers are anionic or nonionic, although the other types may also be used.

[0035] Lotions and creams can be formulated as emulsions as well as solutions. Preferably such lotions comprise from 0.1% to 20%, more preferably from 1% to 5%, of the active compound; from 1% to 20%, preferably from 5% to 10%, of an emollient; from 25% to 75%, preferably from 45% to 95%, water; and from 0.1% to 10%, preferably from 0.5% to 5%, of an emulsifier. Such creams would preferably comprise from 0.1% to 20%, more preferably from 1% to 5%, of the active compound; from 1% to 20%, preferably from 5% to 10%, of an emollient; from 20% to 80%, preferably from 30% to 70%, water; and from 1% to 10%, preferably from 2% to 5%, of an emulsifier.

[0036] Single emulsion skin care preparations, such as lotions and creams, of the oil-in-water type and water-in-oil type are well-known in the cosmetic art and are useful in the present invention. Multiphase emulsion compositions, such as the water-in-oil-in-water type, as disclosed in US-A-4,254,105, Fakuda et al., issued March 3, 1981, are also useful in the present invention. In general, such single or multiphase emulsions contain water, emollients and emulsifiers as essential ingredients.

[0037] Triple emulsion carrier systems comprising an oil-in-water-in-silicone fluid emulsion composition as disclosed in US-A-4,960,764, Figueroa, issued October 2, 1990, are also useful in the present invention. Preferably, this triple emulsion carrier system can be combined with from 0.1% to 20%, more preferably from 1% to 5%, of the active compound to yield the topical pharmaceutical composition of the present invention.

[0038] Another emulsion carrier system useful in the topical pharmaceutical compositions of the present invention is a micro-emulsion carrier system. Such a system comprises from 9% to 15% squalane; from 25% to 40% silicone oil; from 8% to 20% of a fatty alcohol; from 15% to 30% of polyoxyethylene sorbitan mono-fatty acid (commercially available under the trade name Tweens) or other nonionics; and from 7% to 20% water. This carrier system is preferably combined with from 1% to 5% of the active compound.

[0039] If the topical pharmaceutical compositions of the present invention are formulated as a gel or a cosmetic stick, a suitable amount of a thickening agent, as disclosed supra, is added to a cream or lotion formulation.

[0040] The topical pharmaceutical compositions of the present invention may also be formulated as makeup products such as foundations.

[0041] The topical pharmaceutical compositions of the present invention may also be formulated as medicated pads. Suitable examples of these pads are fully disclosed in US-A-4,891,227 and US-A-4,891,228, to Thaman et al., both issued January 2, 1990.

[0042] The topical pharmaceutical compositions of the present invention may contain, in addition to the aforementioned components, a wide variety of additional oil-soluble materials and/or water-soluble materials conventionally used in topical compositions. at their art-established levels.

[0043] Various water-soluble materials may also be present in the compositions of this invention. These include humectants, proteins and polypeptides, preservatives and an alkaline agent. In addition, the topical compositions herein can contain conventional cosmetic adjuvants, such as dyes, opacifiers (e.g., titanium dioxide), pigments and perfumes.

[0044] The topical pharmaceutical compositions of the present invention may also include a safe and effective amount of a penetration enhancing agent. A preferred amount of penetration enhancing agent is from 1% to 5% of the composition. Another useful penetration enhancer for the present invention is the non-ionic polymer under the CTFA designation: polyacrylamide and isoparrafin and laureth-7, available as Sepigel from Seppic Corporation. Also useful is polyquaternium-32 and mineral oil known as SalCare SC92 available from Allied Colloids, Suffolk, VA. This is a class of cationic polymers which are generally described in US-A-4,628,078 to Glover et al. issued December 9, 1986 and US-A-4,599,379 to Flesher et al. issued July 8, 1986.

[0045] Examples of useful penetration enhancers, among others, are disclosed in US-A-4,537,776, Cooper, issued August 27, 1985; US-A-4,552,872, Cooper et al., issued November 12, 1985; US-A-4,557,934, Cooper, issued December 10, 1985; US-A-4,130,667, Smith, issued December 19, 1978; US-A-3,989,816, Rhaadhyaksha, issued November 2, 1976; US-A-4,017,641, DiGiulio, issued April 12, 1977; and EP-A-0043738, Cooper et al., published January 13, 1982.

[0046] Other conventional skin care product additives may also be included in the compositions of the present invention. For example, collagen, hyaluronic acid, elastin, hydrolysates, primrose oil, jojoba oil, epidermal growth factor, soybean saponins, mucopolysaccharides, and mixtures thereof may be used.

Vitamins

[0047] Various vitamins may also be included in the compositions of the present invention. For example, Vitamin A, ascorbic acid, Vitamin B, biotin, panthothenic acid, Vitamin D, Vitamin E and mixtures thereof and derivatives thereof may be used.

Cleaning Compositions

[0048] The skin cleaning compositions of the present invention comprise, in addition to the active compound, a cosmetically-acceptable surfactant. The term "cosmetically-acceptable surfactant" refers to a surfactant which is not only an effective skin cleanser but also can be used without undue toxicity, irritation, allergic response, and the like. Furthermore, the surfactant must be capable of being commingled with the active compound in a manner such that there is no interaction which would substantially reduce the efficacy of the composition for regulating skin atrophy.

[0049] The skin cleaning compositions of the present invention preferably contain from 0.1% to 20%, preferably from 1% to 5%, of the active compound and from 1% to 90%, more preferably from 1% to 10%, of a cosmetically-acceptable surfactant.

[0050] The physical form of the skin cleansing compositions is not critical. The compositions can be, for example, formulated as toilet bars, liquids, pastes, mousses, or pads.

[0051] The surfactant component of the compositions of the present invention are selected from anionic, nonionic, zwitterionic, amphoteric and ampholytic surfactants, as well as mixtures of these surfactants. Such surfactants are well-known to those skilled in the detergency art.

[0052] The cleaning compositions of the present invention can optionally contain, at their art-established levels, materials which are conventionally used in skin cleansing compositions.

Combination Actives

A. Sunscreens and Sunblocks

[0053] Optimum regulation of skin wrinkling resulting from exposure to U.V. light can be obtained by using a combi-

nation of the salicylic acid active of the present invention together with sunscreens or sunblocks. Useful sunblocks include, for example, zinc oxide and titanium dioxide.

[0054] Photodamage is a predominant cause of skin wrinkling. Thus, for purposes of wrinkle prevention, the combination of the active compound with a UVA and/or UVB sunscreen would be most desirable. The inclusion of sunscreens in compositions of the present invention will provide immediate protection against acute UV damage. Thus, the sunscreen will prevent further wrinkle formation caused by UV radiation, while the active compound regulates existing wrinkles and skin atrophy.

[0055] A wide variety of conventional sunscreening agents are suitable for use in combination with the active compound. Segarin, et al., at Chapter VIII, pages 189 et seq., of Cosmetics Science and Technology, disclose numerous suitable agents. Specific suitable sunscreening agents include, for example: p-aminobenzoic acid, its salts and its derivatives (ethyl, isobutyl, glyceryl esters; p-dimethylaminobenzoic acid); anthranilates (i.e., o-aminobenzoates; methyl, menthyl, phenyl, benzyl, phenylethyl, linalyl, terpinyl, and cyclohexenyl esters); salicylates (amyl, phenyl, benzyl, menthyl, glyceryl, and dipropyleneglycol esters); cinnamic acid derivatives, (methyl and benzyl esters, α-phenyl cinnamonitrile; butyl cinnamoyl pyruvate); Dihydroxycinnamic acid derivatives (umbelliferone, methylumbelliferone, methylaceto-umbelliferone); trihydroxycinnamic acid derivatives (esculetin, methylesculetin, daphnetin, and the glucosides, esculin and daphnin); hydrocarbons (diphenylbutadiene, stilbene); dibenzalacetone and benzalacetophenone; Naphtholsulfonates (sodium salts of 2-naphthol-3,6-disulfonic and of 2-naphthol-6,8-disulfonic acids); Dihydroxy-naphthoic acid and its salts; o- and p-Hydroxybiphenyldisulfonates; Coumarin derivatives (7-hydroxy, 7-methyl, 3-phenyl); Diazoles (2-acetyl-3-bromoindazole, phenyl benzoxazole, methyl naphthoxazole, various aryl benzothiazoles); Quinine salts (bisulfate, sulfate, chloride, oleate, and tannate); Quinoline derivatives (8-hydroxyquinoline salts, 2-phenylquinoline); Hydroxy- or methoxy-substituted benzophenones; Uric and vilouric acids; Tannic acid and its derivatives (e.g., hexaethylether); (Butyl carbotol) (6-propyl piperonyl) ether; Hydroquinone; Benzophenones (Oxybenzene, Sulisobenzone, Dioxybenzone, Benzoresorcinol, 2,2',4,4'-Tetrahydroxybenzophenone, 2,2'-Dihydroxy-4,4'-dimethoxybenzophenone, Octabenzone; 4-Isopropyldibenzoylmethane; Butylmethoxydibenzoylmethane; Etocrylene; and 4-isopropyldi-benzoylmethane.

[0056] Preferred sunscreens useful in the compositions of the present invention are 2-ethylhexyl -p-methoxycinnamate, butylmethoxydibenzoylmethane, 2-hydroxy-4-methoxybenzophenone, octyldimethyl-p-aminobenzoic acid and mixtures thereof.

[0057] A safe and effective amount of sunscreen may be used in the compositions of the present invention. The sunscreening agent must be compatible with the active compound. Generally the composition may comprise from 1% to 20%, preferably from 2% to 10%, of a sunscreening agent. Exact amounts will vary depending upon the sunscreen chosen and the desired Sun Protection Factor (SPF).

[0058] Also particularly useful in the present invention are sunscreens such as those disclosed in Sabatelli, US-A-4 937 370 and Sabatelli et al., US-A-4 999 186. The sunscreening agents disclosed therein have, in a single molecule, two distinct chromophore moieties which exhibit different ultra-violet radiation absorption spectra. One of the chromophore moieties absorbs predominantly in the UVB radiation range and the other absorbs strongly in the UVA radiation range.

[0059] An agent may also be added to any of the compositions of the present invention to improve the skin substantivity of those compositions, particularly to enhance their resistance to being washed off by water, or rubbed off. A preferred agent which will provide this benefit is a copolymer of ethylene and acrylic acid. Compositions comprising this copolymer are disclosed in US-A-4,663,157, Brock, issued May 5, 1987.

B. Anti-Inflammatory Agents

[0060] In a preferred atrophy regulating composition of the present invention, an anti-inflammatory agent is included as an active agent along with the active compound. The inclusion of an anti-inflammatory agent enhances the wrinkle regulating benefits of the compositions. The anti-inflammatory agent protects strongly in the UVA radiation range (though it also provides some UVB protection as well) thereby preventing further wrinkle formation caused by UV radiation, while the active compound regulates existing wrinkles and skin atrophy. Thus the combination provides broad protection. The topical use of anti-inflammatory agents reduces photo-aging of the skin resulting from chronic exposure to UV radiation. (See US-A-4,847,071, Bissett, Bush, and Chatterjee, issued July 11, 1989; and US-A-4,847,069, Bissett and Chatterjee, issued July 11, 1989).

[0061] A safe and effective amount of an anti-inflammatory agent may be added to the compositions of the present invention, preferably from 0.1% to 10%, more preferably from 0.5% to 5%, of the composition. The exact amount of anti-inflammatory agent to be used in the compositions will depend on the particular anti-inflamatory agent utilized since such agents vary widely in potency.

[0062] Steroidal anti-inflammatory agents, including but not limited to, corticosteroids such as hydrocortisone, hydroxyltriamcinolone, alpha-methyl dexamethasone, dexamethasone-phosphate, beclomethasone dipropionate;

clobetasol valerate, desonide, desoxymethasone, desoxycorticosterone acetate, dexamethasone, dichlorisone, diflorasone diacetate, diflucortolone valerate, fluadrenolone, fluclorolone acetonide, fludrocortisone, flumethasone pivalate, fluosinolone acetonide, fluocinonide, flucortine butylester, fluocortolone, fluprednidene (fluprednylidene) acetate, flurandrenolone, halcinonide, hydrocortisone acetate, hydrocortisone butyrate, methylprednisolone, triamcinolone acetonide, cortisone, cortodoxone, flucetonide, fludrocortisone, difluorosone diacetate, fluradrenolone acetonide, medrysone, amcinafel, amcinafide, betamethasone and the balance of its esters, chloroprednisone, chlorprednisone acetate, clocortelone, clescinolone, dichlorisone, difluprednate, flucloronide, flunisolide, fluoromethalone, fluperolone, fluprednisolone, hydrocortisone valerate, hydrocortisone cyclopentylpropionate, hydrocortamate, meprednisone, paramethasone, prednisolone, prednisone, beclomethasone dipropionate, triamcinolone, and mixtures thereof may be used. The preferred steroidal anti-inflammatory for use in the present invention is hydrocortisone.

[0063] A second class of anti-inflammatory agents which is useful in the compositions of the present invention includes the nonsteroidal anti-inflammatory agents. The variety of compounds encompassed by this group are well-known to those skilled in the art. For detailed disclosure of the chemical structure, synthesis, side effects, etc., of nonsteroidal anti-inflammatory agents, reference may be had to standard texts, including Antiinflammatory and Anti-Rheumatic Drugs, K. D. Rainsford, Vol. I-III, CRC Press, Boca Raton, (1985), and Anti-inflammatory Agents, Chemistry and Pharmacology, 1, R. A. Scherrer, et al., Academic Press, New York (1974).

[0064] Specific non-steroidal anti-inflammatory agents useful in the composition of the present invention include, but are not limited to:

1) the oxicams, such as piroxicam, isoxicam, tenoxicam, sudoxicam, and CP-14,304;
2) the salicylates, such as aspirin, disalcid, benorylate, trilisate, safapryn, solprin, diflunisal, and fendosal;
3) the acetic acid derivatives, such as diclofenac, fenclofenac, indomethacin, sulindac, tolmetin, isoxepac, furofenac, tiopinac, zidometacin, acomatactn, fentiazac, zomepiract, clidanac, oxepinac, and felbinac;
4) the fenamates, such as mefenamic, meclofenamic, flufenamic, niflumic, and tolfenamic acids;
5) the propionic acid derivatives, such as ibuprofen, naproxen, benoxaprofen, flurbiprofen, ketoprofen, fenoprofen, fenbufen, indoprofen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, and tiaprofenic; and
6) the pyrazoles, such as phenybutazone, oxyphenbutazone, feprazone, azapropazone, and trimethazone.

Mixtures of these non-steroidal anti-inflammatory agents may also be employed, as well as the pharmaceutically-acceptable salts and esters of these agents. For example, etofenamate, a flufenamic acid derivative, is particularly useful for topical application. Of the nonsteroidal anti-inflammatory agents, ibuprofen, naproxen, flufenamic acid, mefenamic acid, meclofenamic acid, piroxicam and felbinac are preferred; ibuprofen, naproxen, and flufenamic acid are most preferred.

[0065] Another class of anti-inflammatory agents which are useful in the present invention are the anti-inflammatory agents disclosed in US-A-4,708,966, Loomans et al., issued November 24, 1987. This patent discloses a class of nonsteroidal anti-inflammatory compounds which comprise specifically substituted phenyl compounds, especially substituted 2,6-di- tert-butyl phenol derivatives. For example, compounds selected from 4 -(4'-pentyn-3'-one)-2,6-di-t-butylphenol; 4-(5'-hexynoyl)-2,6-di-t-butylphenol; 4-((S)-(-)-3'-methyl-5'-hexynoyl)-2,6-di-t-butylphenol; 4-((R)-(+)-3'-methyl-5'-hexynoyl)-2,6-di-t-butylphenol; and 4-(3',3'-dimethoxypropionyl)-2,6-di-t-butylphenol are useful in the present invention.

[0066] Yet another class of anti-inflammatory agents which are useful in the present invention are those disclosed in US-A-4,912,248, Mueller, issued March 27, 1990. This patent discloses compounds and diastereomeric mixtures of specific 2-naphthyl-containing ester compounds, especially naproxen ester and naproxol ester compounds, having two or more chiral centers.

[0067] Finally, so-called "natural" anti-inflammatory agents are useful in the present invention. For example, candelilla wax, alpha bisabolol, aloe vera, Hanjistha (extracted from plants in the genus Rubia, particularly Rubia Cordifolia), and Guggal (extracted from plants in the genus Commiphora, particularly Commiphora Mukul), may be used.

C. Anti-Oxidants/Radical Scavengers

[0068] In a preferred atrophy regulating composition of the present invention, an anti-oxidant/radical scavenger is included as an active agent along with the active compound. The inclusion of an anti-oxidant/radical scavenger increases the wrinkle regulating benefits of the composition.

[0069] A safe and effective amount of an anti-oxidant/radical scavenger may be added to the compositions of the present invention. preferably from 0.1% to 10%, more preferably from 1% to 5%, of the composition.

[0070] Anti-oxidants/radical scavengers such as ascorbic acid (vitamin C) and its salts, tocopherol (vitamin E), tocopherol sorbate, other esters of tocopherol, butylated hydroxy benzoic acids and their salts, 6-hydroxy-2,5,7,8-te-

tramethylchroman-2-carboxylic acid (commercially available under the tradename Trolox®), gallic acid and its alkyl esters, especially propyl gallate, uric acid and its salts and alkyl esters, sorbic acid and its salts, the ascorbyl esters of fatty acids, amines (e.g., N,N-diethylhydroxylamine, amino-guanidine), sulfhydryl compounds (e.g., glutathione), and dihydroxy fumaric acid and its salts may be used.

D. Chelators

[0071] In a preferred atrophy regulating composition of the present invention, a chelating agent is included as an active agent along with the active compound. As used herein, 'chelating agent" means an active agent capable of removing a metal ion from a system by forming a complex so that the metal ion cannot readily participate in or catalyze chemical reactions. The inclusion of a chelating agent increases the wrinkle regulating benefits of the composition.

[0072] A safe and effective amount of a chelating agent may be added to the compositions of the present invention, preferably from 0.1% to 10%, more preferably from 1% to 5%, of the composition. Chelators useful in compositions of the present invention are disclosed in EP-A-0 313 305, Bissett, Bush & Chatterjee. Preferred chelators useful in compositions of the present invention are furildioxime and derivatives thereof, more preferably amphi-2-furildioxime.

E. Retinoids

[0073] In a preferred atrophy regulating composition of the present invention, a retinoid, preferably retinoic acid, is included as an active agent along with the active compound. The inclusion of a retinoid increases the wrinkle regulating benefits of the composition. A safe and effective amount of a retinoid may be added to the compositions of the present invention, preferably from 0.001% to 2%, more preferably from 0.01% to 1% of the composition. As used herein, "retinoid" includes all natural and/or synthetic analogs of Vitamin A or retinal-like compounds which possess the biological activity of Vitamin A in the skin as well as the geometric isomers and stereoisomers of these compounds, such as all-trans retinoic acid and 13-cis-retinoic acid.

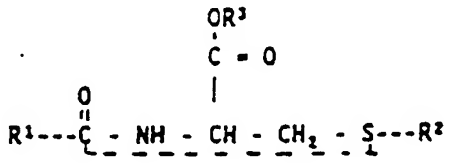
F. Benzofuran Derivatives

[0074] In a preferred atrophy regulating composition of the present invention, a benzofuran derivative, preferably amiodarone, is included as an active agent along with the active compound. The inclusion of a benzofuran derivative increases the wrinkle regulating benefits of the composition.

[0075] A safe and effective amount of a benzofuran derivative may be added to the compositions of the present invention, preferably from 0.01% to 20%, more preferably from 0.1% to 10%, of the composition. Benzofuran derivatives useful in the present invention are disclosed in WO92/07559 Chatterjee and Kapoor.

G. N-acetyl-L-cysteine Derivatives

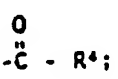
[0076] Also preferred for use herein are compounds having the structure



or a pharmaceutically-acceptable salt thereof.

[0077] R^1 is selected from nil and a C_1-C_{18} alkyl, preferably C_1-C_7, more preferably C_1-C_3, more preferably still C_1 alkyl.

[0078] R^2 is selected from nil, -H, C_1-C_{18} alkyl and



preferably -H and, C_1-C_{18} alkyl, more preferably -H. In one embodiment, R^2 is preferably a C_1-C_{18} alkyl, more preferably C_1-C_7, more preferably C_1-C_3, more preferably still C_1.

[0079] R^3 is selected from -H, and C_1-C_{18} alkyl, preferably -H. In one embodiment, R^3 is preferably a C_1-C_{18} alkyl, more preferably C_1-C_7, more preferably C_1-C_3, more preferably still C_1.

[0080] R^4 is a C_1-C_{18} alkyl; preferably C_1-C_7; more preferably C_1-C_3; more preferably still C_1.

[0081] In another embodiment, both R^1 and R^2 are nil and the carbonyl carbon and the sulfur adjacent R^1 and R^2, respectively, are covalently bonded to form a cyclic ring. Otherwise, both R^1 and R^2 are other than nil.

[0082] Preferred pharmaceutically-acceptable salts of the active compound include, but are not limited to, sodium, potassium, magnesium, calcium, lithium, rubidium, strontium, aluminum, boron, silicon and zinc salts of the active compound.

[0083] Compositions of the present invention comprise from 0.01% to 50% of the active compound, preferably from 0.1% to 20%, more preferably from 2% to 5%.

[0084] Zinc complexes which may be formed by zinc and the active compound are useful in the compositions and methods of the present invention.

H. Skin Protectants

[0085] In a preferred atrophy regulating composition of the present invention, a safe and effective amount of a skin protectant may be added to the compositions of the present invention, the skin protectant preferably comprises from 0.001% to 2%, more preferably from 0.01% to 1% of the composition. Useful skin protectants are disclosed in the Federal Register Vol. 48, No. 32 and include allantoin, aluminum hydroxide gel, bismuth subnitrate, boric acid, calamine, cocoa butter, corn starch, dimethicone, glycerin, kaolin, live yeast cell derivative, petrolatum, shark liver oil, sodium bicarbonate, sulfur, tannic acid, white petrolatum, zinc acetate, zinc carbonate and zinc oxide and mixtures thereof.

[0086] Other useful components include hormones such as pregnenolone and estrogens. Also useful are the alpha-, or beta-hydroxy acids or alpha-keto acids or derivatives thereof as disclosed in US-A-4,234,599 to Van Scott et al., issued November 18, 1980. Useful members of this class include alpha-hydroxy-butyric acid, alpha-hydroxyisobutyric acid, alpha-hydroxyisocaproic acid, alpha-hydroxyisovaleric, atrolactic acid, beta-hydroxybutyric acid, beta-phenyl lactic acid, beta-phenylpyruvic acid, citric acid ethyl pyruvate, galacturonic acid, glucoheptonic acid, glucoheptono 1,4-lactone, gluconic acid, gluconolactone glucuronic acid, glucuronolactone, glycolic acid, isopropyl pyruvate, lactic acid, malic acid, amndelic acid, emthyl pyruvate, mucic acid, pyruvic acid, saccharic acid, saccharic acid 1,4-lactone, tartaric acid and tartronic acid.

Cosmetic Methods for Regulating Skin Atrophy in Mammalian Skin

[0087] The present invention relates to a cosmetic method for regulating atrophy in mammalian skin. Such a method comprises treating the skin with a safe and effective amount of the active compound. The amount of active compound and frequency of treatment will vary widely depending upon the level of skin atrophy already in existence in the subject, the rate of further atrophy, and the level of regulation desired.

[0088] A preferred method of treating the skin is via chronic topical application of a safe and effective amount of the active compound to regulate atrophy in mammalian skin. The amount of active compound and frequency of topical application to the skin can vary widely, depending upon personal needs, but it is suggested as an example that topical application range from about once per week to about 10 times daily, preferably from about twice per week to about 4 times daily, more preferably from about 3 times a week to about 3 times daily, most preferably about once or twice per day. The composition for topical application will comprise from 0.01% to 50%, preferably from 0.1% to 20%, more preferably from 1% to 5% of the active compound. By "chronic" application, it is meant herein that the period of topical application may be over the lifetime of the subject, preferably for a period of at least about three weeks, more preferably from about three months to about twenty years, more preferably from about six months to about ten years, more preferably still from about one year to about five years, thereby resulting in regulation of atrophy in mammalian skin.

[0089] A preferred cosmetic method of the present invention for regulating atrophy in mammalian skin involves applying both a safe and effective amount of the active compound and a safe and effective amount of one or more of a sunscreening agent, anti-inflammatory agent, Vitamin, anti-oxidant/radical scavenging agent, chelating agent, retinoid, N-acetyl-L-cysteine derivative, skin protectant and/or benzofuran derivative to the skin simultaneously. As used herein, "simultaneous application" or "simultaneously" means applying the agents to the skin at the same situs on the body at about the same time. Though this can be accomplished by applying the agents separately to the skin, preferably a composition comprising all the desired agents commingled is applied to the skin. The amount of sunscreening agent applied is generally from 0.02 mg to 1.0 mg per cm^2 skin. The amount of anti-inflammatory agent applied is generally from 0.005 mg to 0.5 mg, preferably from 0.01 mg to 0.1 mg per cm^2 skin. The amount of anti-oxidant/radical scavenging agent generally applied is from 0.001 mg to 1.0 mg, preferably from 0.05 mg to 0.5 mg per cm^2 skin. The amount of chelating agent generally applied is from .001 mg to 1.0 mg, preferably from 0.01 mg to 0.5 mg, more preferably from 0.05 mg to 0.1 mg per cm^2 skin. The amount of retinoid applied is generally from 0.00001 mg to 0.02 mg per cm^2 skin,

preferably from 0.001 mg to 0.01 mg per cm^2 skin. The amount of benzofuran derivative applied is generally from 0.001 mg to 1.0 mg/cm^2 skin per application, preferably from 0.01 to 0.5 mg/cm^2 skin per application. The amount of active compound applied is generally from 0.001 mg to 1.0 mg per cm^2 skin per application, preferably from 0.01 mg to 0.5 mg per cm^2, more preferably from 0.05 to 0.25 mg/cm^2 skin per application.

[0090] The following examples further describe and demonstrate the preferred embodiments within the scope of the present invention.

EXAMPLE I

[0091] A pad of the present invention is made as follows:

Pad Composition	Weight %
Substrate A	
Cellulose-based nonwoven[1]	100.0
Substrate B	
Polyester 54 tex (denier = 6)[2]	45.0
Orlon 72 tex (denier = 8)[3]	15.0
Styrene-butadiene resin[4]	40.0
Laminate	
Polyethylene Powder Melt[5]	100.0
Active Composition	**Weight %**
Salicylic acid	2.0
Na Methyl cocoyl taurate	3.0
C_2H_5OH (95% ethanol)	35.0
Witch Hazel distillate	5.0
Quaternium-22	1.0
Menthol	0.1
Aloe Vera Gel	0.5
Fragrance	0.05
Water	q.s.

[1] Obtained from James River as Airtex Spec 382.
[2] Obtained from Eastern Chemical Company.
[3] Obtained from American Cyanamid.
[4] Obtained from Reichold as tylac 68-500 (ratio of styrene to butadiene 80:20).
[5] Obtained from Quantum Chemical as microthene powder.

[0092] Substrate A has a basis weight of about 55 grams per square yard and a loft of about 35 mills. Substrate B has a basis weight of about 65 grams per square yard and a loft of about 70 to 80 mills. The two materials are laminated together by applying a thin coat of Polyethylene power to Substrate A and heating with IR lamps. Substrate A and B are then joined at a hip roll to compress and bond the materials. The resulting nonwoven fabric has a loft of about 90 to 100 mills. The resulting material is then cut into an oval shape (5 cm. x 7 cm.). The active components are combined to form a solution and the pad composition is saturated in this solution.

[0093] This composition is useful for topical application to regulate skin atrophy. Use of an amount of the composition to deposit about 2 mg/cm^2 of the active compound to the skin is appropriate.

EXAMPLE II

[0094] A pad of the present invention is made by combining the following components as in Example I:

Pad Composition	Weight %
Substrate A	
Cellulose-based nonwoven	100.0
Substrate B	
Polyester 54 tex (denier = 6)	45.0
Orlon 72 tex (denier = 8)	15.0
Styrene-butadiene resin	40.0
Laminate	
Polyethylene Powder Melt	100.0
Active Composition	**Weight %**
Salicylic acid	2.0
C_2H_5OH (95% ethanol)	35.0
Glycerin	2.0
Aloe Vera Gel	1.0
Menthol	0.05
Triethanol Amine	0.7
Fragrance	0.15
Water	q.s.

[0095] This composition is useful for topical application to regulate skin atrophy. Use of an amount of the composition to deposit about 2 mg/cm^2 of the active compound to the skin is appropriate.

EXAMPLE III

[0096] A topical composition is prepared by combining the following components utilizing conventional mixing techniques.

Active Composition	Weight %
Salicylic acid,	1.25
Ascorbic acid	5.00
Na Methyl cocoyl taurate	1.5
C_2H_5OH (95% ethanol)	45.0
Witch Hazel distillate	5.0
Quaternium-22	1.0
Menthol	0.05
Fragrance	0.05
Water	41.15

[0097] This composition is useful for topical application to regulate skin atrophy. Use of an amount of the composition to deposit about 2 mg/cm^2 of the active compound to the skin is appropriate.

EXAMPLE IV

[0098] A topical composition is made by combining the following components using conventional mixing technology.

Ingredient	W/W%
Water, Purified	54.0

(continued)

Ingredient	W/W%
Alcohol SD 40	40.0
Polyacrylamide and C_{13-14} Isoparaffin and Laureth-7[1]	4.0
Salicylic Acid	2.0

[1]Available as Sepigel from Seppic Corporation.

Water is added to a suitable size container. While mixing at a moderate speed (300 rpm), the polyacrylamide isoparaffin and laureth-7 is added to the water. Separately, the alcohol is placed in a container and covered. Using a Lightnin' Mixer with a 3 blade paddle prop, the salicylic acid is added to the alcohol and mixed at a low speed (100 rpm) until all salicylic acid is dissolved. The alcohol is slowly added to the water phase to form a gel. The resulting gel is mixed at moderate speed until uniform.

[0099] This composition is useful for topical application to regulate skin atrophy. Use of an amount of the composition to deposit about 2 mg/cm^2 of the active compound to the skin is appropriate.

EXAMPLE V

[0100] A topical composition is made by combining the following components using conventional mixing technology as in Example IV.

Ingredient	W/W%
Water	q.s.
Alcohol SD 40	40.0
Salcare SC92[1]	3.0
Salicylic Acid	2.0
Menthol	0.05
N_{92}EDTA	0.05
Glycerin	2.00

[1]Salcare SC92 is a copolymer of acylamide and a cationic acrylate available from Allied Colloids.

[0101] This composition is useful for topical application to regulate skin atrophy. Use of an amount of the composition to deposit about 2 mg/cm^2 of the active compound to the skin is appropriate.

Claims

1. The use of a safe and effective amount of salicylic acid and a pharmaceutically-acceptable hydroalcoholic carrier in a composition for treating the skin to regulate atrophy excluding methods for treatment of the human or animal body by surgery or therapy or diagnostic methods.

2. The use of Claim 1 wherein the composition comprises from 0.01% to 50% of salicylic acid, preferably from 0.1% to 20% of salicylic acid.

3. The use of Claim 2 wherein the pharmaceutically-acceptable carrier is a topical carrier, preferably wherein the topical carrier comprises:

   (a) from 10 to 60 weight percent of C_2H_5OH or C_3H_7OH;
   (b) from 30 to 80 weight percent of water;
   and
   (c) from 0.2 to 5.0 weight percent of sodium methyl cocoyl taurate or sodium methyl oleoyl taurate; the composition having a pH value of from 2 to 3.5.

4. The use of Claim 3 wherein the treatment of the skin with the composition is chronic, or wherein the treatment of the skin with the composition is for a period of at least about three weeks comprising application of the composition

from about once per week to about two times daily.

5. The use of Claim 4 wherein the composition additionally comprises a safe and effective amount of a sunscreening agent, preferably wherein said sunscreening agent is selected from 2-ethylhexyl-p-methoxycinnamate, butyl-methoxydibenzoylmethane, 2-hydroxy-4-methoxybenzophenone, octyldimethyl-p-aminobenzoic acid and mixtures thereof.

6. The use of Claim 4 wherein the composition additionally comprises another active agent selected from a safe and effective amount of an anti-inflammatory agent, vitamins, an anti-oxidant, a chelator, a retinoid, a benzufuran derivative, an N-acetyl-L-cysteine derivative and a skin protectant and mixtures thereof.

7. The use of Claim 5 wherein said anti-inflammatory agent is selected from hydrocortisone, hydroxyltriamcinolone, alpha-methyl dexamethasone, dexamethasone-phosphate, beclomethasone dipropionate, clobetasol valerate, desonide, desoxymethasone, desoxycorticosterone acetate, dexamethasone, dichlorisone, diflorasone diacetate, diflucortolone valerate, fluadrenolone, fluclorolone acetonide, fludrocortisone, flumethasone pivalate, fluosinolone acetonide, fluocinonide, flucortine butylester, fluocortolone, fluprednidene (fluprednylidene) acetate, flurandrenolone, halcinonide, hydrocortisone acetate, hydrocortisone butyrate, methylprednisolone, triamcinolone acetonide, cortisone, cortodoxone, flucetonide, fludrocortisone, difluorosone diacetate, fluradrenolone acetonide, medrysone, amcinafel, amcinafide, betamethasone and the balance of its esters, chloroprednisone, chlorprednisone acetate, clocortelone, clescinolone, dichlorisone, difluprednate, flucloronide, flunisolide, fluoromethalone, fluperolone, fluprednisolone, hydrocortisone valerate, hydrocortisone cyclopentylpropionate, hydrocortamate, meprednisone, paramethasone, prednisolone, prednisone, beclomethasone dipropionate, triamcinolone, piroxicam, isoxicam, tenoxicam, sudoxicam, CP-14,304, aspirin, disalcid, benorylate, trilisate, safapryn, solprin, diflunisal, and fendosal, diclofenac, fenclofenac, indomethacin, sulindac, tolmetin, isoxepac, furofenac, tiopinac, zidometacin, acematacin, fentiazac, zomepiract, clidanac, oxepinac, and felbinac, mefenamic, meclofenamic, flufenamic, niflumic, and tolfenamic acid, ibuprofen, naproxen, benoxaprofen, flurbiprofen, ketoprofen, fenoprofen, fenbufen, indoprofen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, and tiaprofenic, phenybutazone, oxyphenbutazone, feprazone, azapropazone, and trimethazone and mixtures thereof.

8. The use of Claim 5 wherein said anti-oxidant or radical scavenger is selected from ascorbic acid, tocopherol, butylated hydroxy benzoic acids, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, gallic acid, uric acid, sorbic acid, N,N-diethylhydroxylamine, amino-guanidine), sulfhydryl compounds, and dihydroxy fumaric acid, derivatives thereof and mixtures thereof.

9. The use of Claim 5 wherein said retinoid is selected from all-trans retinoic acid and 13-cis-retinoic acid and mixtures thereof.

10. The use of Claim 5 wherein said skin protectant is selected from allantoin, aluminum hydroxide gel, bismuth subnitrate, boric acid, calamine, cocoa butter, corn starch, dimethicone, glycerin, kaolin, live yeast cell derivative, petrolatum, shark liver oil, sodium bicarbonate, sulfur, tannic acid, white petrolatum, zinc acetate, zinc carbonate and zinc oxide and mixtures thereof.

11. A cosmetic method for regulating atrophy in mammalian skin comprising treating the skin with a safe and effective amount of a composition comprising:

(a) a safe and effective amount of salicylic acid; and

(b) a hydroalcoholic pharmaceutically-acceptable carrier excluding methods for treatment of the human or animal body by surgery or therapy or diagnostic methods.

12. The method of Claim 11 wherein the composition comprises from 0.01% to 50% of salicylic acid, preferably from 0.1% to 20% of salicylic acid.

13. The method of Claim 12 wherein the pharmaceutically-acceptable carrier is a topical carrier, preferably wherein the topical carrier comprises:

(a) from 10 to 60 weight percent of C_2H_5OH or C_3H_7OH;
(b) from 30 to 80 weight percent of water;

and
(c) from 0.2 to 5.0 weight percent of sodium methyl cocoyl taurate or sodium methyl oleoyl taurate; the composition having a pH value of from 2 to 3.5.

14. The method of Claim 13 wherein the treatment of the skin with the composition is chronic, or wherein the treatment of the skin with the composition is for a period of at least about three weeks comprising application of the composition from about once per week to about two times daily.

15. The method of Claim 14 wherein the composition additionally comprises a safe and effective amount of a sunscreening agent, preferably wherein said sunscreening agent is selected from 2-ethylhexyl-p-methoxycinnamate, butylmethoxydibenzoylmethane, 2-hydroxy-4-methoxybenzophenone, octyldimethyl-p-aminobenzoic acid and mixtures thereof.

16. The method of Claim 14 wherein the composition additionally comprises another active agent selected from a safe and effective amount of an anti-inflammatory agent, vitamins, an anti-oxidant, a chelator, a retinoid, a benzufuran derivative, an N-acetyl-L-cysteine derivative and a skin protectant and mixtures thereof.

17. The method of Claim 15 wherein said anti-inflammatory agent is selected from hydrocortisone, hydroxyltriamcinolone, alpha-methyl dexamethasone, dexamethasone-phosphate, beclomethasone dipropionate, clobetasol valerate, desonide, desoxymethasone, desoxycorticosterone acetate, dexamethasone, dichlorisone, diflorasone diacetate, diflucortolone valerate, fluadrenolone, fluclorolone acetonide, fludrocortisone, flumethasone pivalate, fluosinolone acetonide, fluocinonide, flucortine butylester, fluocortolone, fluprednidene (fluprednylidene) acetate, flurandrenolone, halcinonide, hydrocortisone acetate, hydrocortisone butyrate, methylprednisolone, triamcinolone acetonide, cortisone, cortodoxone, flucetonide, fludrocortisone, difluorosone diacetate, fluradrenolone acetamide, medrysone, amcinafel, amcinafide, betamethasone and the balance of its esters, chloroprednisone, chlorprednisone acetate, clocortelone; clescinolone, dichlorisone, difluprednate, flucloronide, flunisolide, fluoromethalone, fluperolone, fluprednisolone, hydrocortisone valerate, hydrocortisone cyclopentylpropionate, hydrocortamate, meprednisone, paramethasone, prednisolone, prednisone, beclomethasone dipropionate, triamcinolone, piroxicam, isoxicam, tenoxicam, sudoxicam,CP-14,304, aspirin, disalcid, benorylate, trilisate, safapryn, solprin, diflunisal, and fendosal, diclofenac, fenclofenac, indomethacin, sulindac, tolmetin, isoxepac, furofenac, tiopinac, zidometacin, acematacin, fentiazac, zomepiract, clidanac, oxepinac, and felbinac, mefenamic, meclofenamic, flufenamic, niflumic, and tolfenamic acid, ibuprofen, naproxen, benoxaprofen, flurbiprofen, ketoprofen, fenoprofen, fenbufen, indoprofen, pirprofen, carprofen, oxaprozin, pranoprofen, miroprofen, tioxaprofen, suprofen, alminoprofen, and tiaprofenic, phenybutazone, oxyphenbutazone, feprazone, azapropazone, and trimethazone and mixtures thereof.

18. The method of Claim 15 wherein said anti-oxidant or radical scavenger is selected from ascorbic acid, tocopherol, butylated hydroxy benzoic acids, 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid, gallic acid, uric acid, sorbic acid, N,N-diethylhydroxylamine, amino-guanidine), sulfhydryl compounds, and dihydroxy fumaric acid, derivatives thereof and mixtures thereof.

19. The method of Claim 15 wherein said retinoid is selected from all-trans retinoic acid and 13-cis-retinoic acid and mixtures thereof.

20. The method of Claim 15 wherein said skin protectant is selected from allantoin, aluminum hydroxide gel, bismuth subnitrate, boric-acid, calamine, cocoa butter, corn starch, dimethicone, glycerin, kaolin, live yeast cell derivative, petrolatum, shark liver oil, sodium bicarbonate, sulfur, tannic acid, white petrolatum, zinc acetate, zinc carbonate and zinc oxide and mixtures thereof.

Patentansprüche

1. Verwendung einer sicheren und wirksamen Menge an Salicylsäure und eines pharmazeutisch annehmbaren hydroalkoholischen Trägers in einer Zusammensetzung zur Behandlung der Haut zur Regulierung von Atrophie, ausgenommen Verfahren zur chirurgischen oder therapeutischen Behandlung des menschlichen oder tierischen Körpers oder Diagnostizierverfahren.

2. Verwendung nach Anspruch 1, wobei die Zusammensetzung 0,01 bis 50% Salicylsäure, vorzugsweise 0,1 bis 20% Salicylsäure enthält.

3. Verwendung nach Anspruch 2, wobei der pharmazeutisch annehmbare Träger ein topischer Träger ist, wobei vorzugsweise der topische Träger umfaßt:

   (a) 10 bis 60 Gew.-% C_2H_5OH oder C_3H_7OH;
   (b) 30 bis 80 Gew.-% Wasser; und
   (c) 0,2 bis 5,0 Gew.-% Natriummethylcocoyltaurat oder Natriummethyloleyltaurat; wobei die Zusammensetzung eine pH-Wert von 2 bis 3,5 aufweist.

4. Verwendung nach Anspruch 3, wobei die Behandlung der Haut mit der Zusammensetzung chronisch erfolgt, oder wobei die Behandlung der Haut mit der Zusammensetzung über einen Zeitraum von mindestens etwa 3 Wochen erfolgt, umfassend die Anwendung der Zusammensetzung von etwa einmal pro Woche bis etwa zweimal täglich.

5. Verwendung nach Anspruch 4, wobei die Zusammensetzung zusätzlich eine sichere und wirksame Menge eines Sonnenschutzmittels umfaßt, wobei das Sonnenschutzmittel vorzugsweise aus 2-Ethylhexyl-p-methoxycinnamat, Butylmethoxydibenzoylmethan, 2-Hydroxy-4-methoxybenzophenon, Octyldimethyl-p-aminobenzoesäure und Mischungen hiervon gewählt ist.

6. Verwendung nach Anspruch 4, wobei die Zusammensetzung zusätzlich einen weiteren Wirkstoff umfaßt, gewählt aus einer sicheren und wirksamen Menge eines antiinflammatorischen Mittels, Vitaminen, einem Antioxidans, einem Chelator, einem Retinoid, einem Benzofuranderivat, einem N-Acetyl-L-cysteinderivat und einem Hautschutzmittel sowie Mischungen hiervon.

7. Verwendung nach Anspruch 5, wobei das antiinflammatorische Mittel gewählt wird aus Hydrocortison, Hydroxyltriamcinolon, alpha-Methyldexamethason, Dexamethason-phosphat, Beclomethasondipropionat, Clobetasolvalerat, Desonid, Desoxymethason, Desoxycorticosteronacetat, Dexamethason, Dichlorison, Diflurasondiacetat, Diflucortolonvalerat, Fluadrenolon, Fluclorolonacetonid, Fludrocortison, Flumethasonpivalat, Fluosinolonacetonid, Fluocinonid, Flucortinbutylester, Fluocortolon, Flupredniden (Fluprednyliden)-acetat, Flurandrenolon, Halcinonid, Hydrocortisonacetat, Hydrocortisonbutyrat, Methylprednisolon, Triamcinolonacetonid, Cortison, Cortodoxon, Flucetonid, Fludrocortison, Difluorosondiacetat, Fluradrenolonacetonid, Medryson, Amcinafel, Amcinafid, Betamethason und dessen restlichen Ester, Chlorprednison, Chlorprednisonacetat, Clocortelon, Clescinolon, Dichlorison, Difluprednat, Flucloronid, Flunisolid, Fluormethalon, Fluperolon, Fluprednisolon, Hydrocortisonvalerat, Hydrocortisoncyclopentylpropionat, Hydrocortamat, Meprednison, Paramethason, Prednisolon, Prednison, Beclomethasondipropionat, Triamcinolon, Piroxicam, Isoxicam, Tenoxicam, Sudoxicam, CP-14,304, Aspirin, Disalcid, Benorylat, Trilisat, Safapryn, Solprin, Diflunisal, und Fendosal, Diclofenac, Fenclofenac, Indomethacin, Sulindac, Tolmetin, Isoxepac, Furofenac, Tiopinac, Zidometacin, Acematacin, Fentiazac, Zomepiract, Clidanac, Oxepinac, und Felbinac, Mefenamic, Meclofenamic, Flufenamic, Niflumic, und Tolfenaminsäure, Ibuprofen, Naproxen, Benoxaprofen, Flurbiprofen, Ketoprofen, Fenoprofen, Fenbufen, Indoprofen, Pirprofen, Carprofen, Oxaprozin, Pranoprofen, Miroprofen, Tioxaprofen, Suprofen, Alminoprofen, und Tiaprofenic, Phenylbutazon, Oxyphenbutazon, Feprazon, Azapropazon, und Trimethazon und Mischungen hiervon.

8. Verwendung nach Anspruch 5, wobei das Antioxidans oder der Radikalfänger aus Ascorbinsäure, Tocopherol, butylierten Hydroxybenzoesäuren, 6-Hydroxy-2,5,7,8-tetramethylchroman-2-carbonsäure, Gallussäure, Harnsäure, Sorbinsäure, N,N-Diethylhydroxylamin, Aminoguanidin, Sulfhydrylverbindungen und Dihydroxyfumarsäure, Derivaten hiervon und Mischungen hiervon gewählt wird.

9. Verwendung nach Anspruch 5, wobei das Retinoid aus all-trans-Retinsäure und 13-cis-Retinsäure und Mischungen hiervon gewählt wird.

10. Verwendung nach Anspruch 5, wobei das Hautschutzmittel aus Allantoin, Aluminiumhydroxidgel, Wismutsubnitrat, Borsäure, Calamin, Kakaobutter, Maisstärke, Dimethicon, Glycerin, Kaolin, lebendem Hefezellenderivat, Petrolatum, Haifischleberöl, Natriumbicarbonat, Schwefel, Tanninsäure, Alvolen, Zinkacetat, Zinkcarbonat und Zinkoxid und Mischungen hiervon gewählt wird.

11. Kosmetisches Verfahren zur Regulierung von Atrophie in der Haut von Säugern, umfassend das Behandeln der Haut mit einer sicheren und wirksamen Menge einer Zusammensetzung, umfassend:

   (a) eine sichere und wirksame Menge Salicylsäure; und
   (b) einen hydroalkoholischen, pharmazeutisch annehmbaren Träger,

ausgenommen Verfahren zur chirurgischen oder therapeutischen Behandlung des meschlichen oder tierischen Körpers oder Diagnostizierverfahren.

12. Verfahren nach Anspruch 11, wobei die Zusammensetzung 0,01 bis 50% Salicylsäure, vorzugsweise 0,1 bis 20% Salicylsäure umfaßt.

13. Verfahren nach Anspruch 12, wobei der pharmazeutisch annehmbare Träger ein topischer Träger ist, wobei vorzugsweise der topische Träger umfaßt:

(a) 10 bis 60 Gew.-% C_2H_5OH oder C_3H_7OH;
(b) 30 bis 80 Gew.-% Wasser; und
(c) 0,2 bis 5,0 Gew.-% Natriummethylcocoyltaurat oder Natriummethyloleyltaurat; wobei die Zusammensetzung einen pH-Wert von 2 bis 3,5 aufweist.

14. Verfahren nach Anspruch 13, wobei die Behandlung der Haut mit der Zusammensetzung chronisch erfolgt, oder wobei die Behandlung der Haut mit der Zusammensetzung über einen Zeitraum von mindestens etwa 3 Wochen erfolgt, umfassend die Anwendung der Zusammensetzung von etwa einmal pro Woche bis etwa zweimal täglich.

15. Verfahren nach Anspruch 14, wobei die Zusammensetzung zusätzlich eine sichere und wirksame Menge eines Sonnenschutzmittels umfaßt, wobei das Sonnenschutzmittel vorzugsweise aus 2-Ethylhexyl-p-methoxycinnamat, Butylmethoxydibenzoylmethan, 2-Hydroxy-4-methoxybenzophenon, Octyldimethyl-p-aminobenzoesäure und Mischungen hiervon gewählt ist.

16. Verfahren nach Anspruch 14, wobei die Zusammensetzung zusätzlich einen weiteren Wirkstoff umfaßt, gewählt aus einer sicheren und wirksamen Menge eines antiinflammatorischen Mittels, Vitaminen, einem Antioxidans, einem Chelator, einem Retinoid, einem Benzofuranderivat, einem N-Acetyl-L-cysteinderivat und einem Hautschutzmittel sowie Mischungen hiervon.

17. Verfahren nach Anspruch 15, wobei das antiinflammatorische Mittel gewählt wird aus Hydrocortison, Hydroxyltriamcinolon, alpha-Methyldexamethason, Dexamethason-phosphat, Beclomethasondipropionat, Clobetasolvalerat, Desonid, Desoxymethason, Desoxycorticosteronacetat, Dexamethason, Dichlorison, Diflurasondiacetat, Diflucortolonvalerat, Fluadrenolon, Fluclorolonacetonid, Fludrocortison, Flumethasonpivalat, Fluosinolonacetonid, Fluocinonid, Flucortinbutylester, Fluocortolon, Flupredniden (Fluprednyliden)-acetat, Flurandrenolon, Halcinonid, Hydrocortisonacetat, Hydrocortisonbutyrat, Methylprednisolon, Triamcinolonacetonid, Cortison, Cortodoxon, Flucetonid, Fludrocortison, Difluorosondiacetat, Fluradrenolonacetonid, Medryson, Amcinafel, Amcinafid, Betamethason und dessen restlichen Ester, Chlorprednison, Chlorprednisonacetat, Clocortelon, Clescinolon, Dichlorison, Difluprednat, Flucloronid, Flunisolid, Fluormethalon, Fluperolon, Fluprednisolon, Hydrocortisonvalerat, Hydrocortisoncyclopentylpropionat, Hydrocortamat, Meprednison, Paramethason, Prednisolon, Prednison, Beclomethasondipropionat, Triamcinolon, Piroxicam, Isoxicam, Tenoxicam, Sudoxicam, CP-14,304, Aspirin, Disalcid, Benorylat, Trilisat, Safapryn, Solprin, Diflunisal, und Fendosal, Diclofenac, Fenclofenac, Indomethacin, Sulindac, Tolmetin, Isoxepac, Furofenac, Tiopinac, Zidometacin, Acematacin, Fentiazac, Zomepiract, Clidanac, Oxepinac, und Felbinac, Mefenamic, Meclofenamic, Flufenamic, Niflumic, und Tolfenaminsäure, Ibuprofen, Naproxen, Benoxaprofen, Flurbiprofen, Ketoprofen, Fenoprofen, Fenbufen, Indoprofen, Pirprofen, Carprofen, Oxaprozin, Pranoprofen, Miroprofen, Tioxaprofen, Suprofen, Alminoprofen, und Tiaprofenic, Phenylbutazon, Oxyphenbutazon, Feprazon, Azapropazon, und Trimethazon und Mischungen hiervon.

18. Verfahren nach Anspruch 15, wobei das Antioxidans oder der Radikalfänger aus Ascorbinsäure, Tocopherol, butylierten Hydroxybenzoesäuren, 6-Hydroxy-2,5,7,8-tetramethylchroman-2-carbonsäure, Gallussäure, Harnsäure, Sorbinsäure, N,N-Diethylhydroxylamin, Aminoguanidin, Sulfhydrylverbindungen und Dihydroxyfumarsäure, Derivaten hiervon und Mischungen hiervon gewählt wird.

19. Verfahren nach Anspruch 15, wobei das Retinoid aus all-trans-Retinsäure und 13-cis-Retinsäure und Mischungen hiervon gewählt wird.

20. Verfahren nach Anspruch 15, wobei das Hautschutzmittel aus Allantoin, Aluminiumhydroxidgel, Wismutsubnitrat, Borsäure, Calamin, Kakaobutter, Maisstärke, Dimethicon, Glycerin, Kaolin, lebendem Hefezellenderivat, Petrolatum, Haifischleberöl, Natriumbicarbonat, Schwefel, Tanninsäure, Alvolen, Zinkacetat, Zinkcarbonat und Zinkoxid und Mischungen hiervon gewählt wird.

Revendications

1. Utilisation d'une quantité sans danger et efficace d'acide salicylique et d'un véhicule hydro-alcoolique acceptable d'un point de vue pharmaceutique, dans une composition destinée au traitement de la peau pour réguler l'atrophie, à l'exclusion des procédés de traitement du corps humain ou animal par chirurgie ou thérapie ou des méthodes de diagnostic.

2. Utilisation selon la revendication 1, dans laquelle la composition comprend de 0,01% à 50% d'acide salicylique, de préférence de 0,1% à 20% d'acide salicylique.

3. Utilisation selon la revendication 2, dans laquelle le véhicule acceptable d'un point de vue pharmaceutique est un véhicule à usage local, de préférence dans laquelle le véhicule à usage local comprend:

   (a) de 10 à 60 pour cent en poids de C_2H_5OH ou C_3H_7OH;
   (b) de 30 à 80 pour cent en poids d'eau; et
   (c) de 0,2 à 5,0 pour cent en poids de méthylalkyl(de coprah)taurate de sodium ou de méthyloléoyltaurate de sodium; la composition ayant un pH de 2 à 3,5.

4. Utilisation selon la revendication 3, dans laquelle le traitement de la peau avec la composition est un traitement chronique, ou dans laquelle le traitement de la peau avec la composition s'effectue pendant une période d'au moins environ trois semaines comprenant l'application de la composition entre environ une fois par semaine et environ deux fois par jour.

5. Utilisation selon la revendication 4, dans laquelle la composition comprend en outre une quantité sans danger et efficace d'un écran solaire, de préférence dans laquelle ledit écran solaire est choisi parmi le p-méthoxycinnamate de 2-éthylhexyle, le butylméthoxydibenzoylméthane, la 2-hydroxy-4-méthoxybenzophénone, l'acide octyldiméthyl-p-aminobenzoïque et leurs mélanges.

6. Utilisation selon la revendication 4, dans laquelle la composition comprend en outre, en une quantité sans danger et efficace, un autre agent actif choisi parmi un agent anti-inflammatoire, des vitamines, un antioxydant, un chélateur, un rétinoïde, un dérivé de benzofurane, un dérivé de N-acétyl-L-cystéine et un protecteur cutané, et leurs mélanges.

7. Utilisation selon la revendication 5, dans laquelle ledit agent anti-inflammatoire est choisi parmi l'hydrocortisone, l'hydroxyltriamcinolone, l'alpha-méthyldexaméthasone, le dexaméthasonephosphate, le dipropionate de béclométhasone, le valérate de clobétasol, le désonide, la désoxyméthasone, l'acétate de désoxycorticostérone, la dexaméthasone, la dichlorisone, le diacétate de diflorasone, le valérate de diflucortolone, la fluadrénolone, le fluclorolone acétonide, la fludrocortisone, le pivalate de fluméthasone, le fluosinolone acétonide, le fluocinonide, l'ester butylique de flucortine, la fluocortolone, l'acétate de fluprednidène (fluprednylidène), la flurandrénolone, l'halcinonide, l'acétate d'hydrocortisone, le butyrate d'hydrocortisone, la méthylprednisolone, le triamcinolone acétonide, la cortisone, la cortodoxone, le flucétonide, la fludrocortisone, le diacétate de difluorosone, le fluradrénolone acétonide, la médrysone, l'amcinafel, l'amcinafide, la bétaméthasone et le restant de ses esters, la chloroprednisone, l'acétate de chlorprednisone, la clocortolone, la clescinolone, la dichlorisone, le difluprednate, le flucloronide, le flunisolide, la fluorométhalone, la flupérolone, la fluprednisolone, le valérate d'hydrocortisone, le cyclopentylpropionate d'hydrocortisone, l'hydrocortamate, la méprednisone, la paraméthasone, la prednisolone, la prednisone, le dipropionate de béclométhasone, la triamcinolone, le piroxicam, l'isoxicam, le ténoxicam, le sudoxicam, CP-14 304, l'aspirine, le disalcide, le bénorylate, le trilisate, la safapryne, la solprine, le diflunisal et le fendosal, le diclofénac, le fenclofénac, l'indométacine, le sulindac, la tolmétine, l'isoxépac, le furofénac, le tiopinac, la zidométacine, l'acématacine, le fentiazac, le zomépiract, le clidanac, l'oxépinac et le felbinac, l'acide méfénamique, méclofénamique, flufénamique, niflumique et tolfénamique, l'ibuprofène, le naproxène, le bénoxaprofène, le flurbiprofène, le kétoprofène, le fénoprofène, le fenbufène, l'indoprofène, le pirprofène, le carprofène, l'oxaprozine, le pranoprofène, le miroprofène, le tioxaprofène, le suprofène, l'alminoprofène, et l'acide tiaprofénique, la phénylbutazone, l'oxyphenbutazone, la féprazone, l'azapropazone et la triméthazone ainsi que leurs mélanges.

8. Utilisation selon la revendication 5, dans laquelle ledit antioxydant ou piégeur de radicaux est choisi parmi l'acide ascorbique, le tocophérol, les acides hydroxybenzoïques butylés, l'acide 6-hydroxy-2,5,7,8-tétraméthylchroman-2-carboxylique, l'acide gallique, l'acide urique, l'acide sorbique, la N,N-diéthylhydroxylamine, l'aminoguanidine, les composés sulfhydryles et l'acide dihydroxyfumarique, leurs dérivés et leurs mélanges.

9. Utilisation selon la revendication 5, dans laquelle ledit rétinoïde est choisi parmi l'acide entièrement-trans-rétinoïque et l'acide 13-cis-rétinoïque et leurs mélanges.

10. Utilisation selon la revendication 5, dans laquelle ledit protecteur cutané est choisi parmi l'allantoïne, le gel d'hydroxyde d'aluminium, le sous-nitrate de bismuth, l'acide borique, la calamine, le beurre de cacao, l'amidon de maïs, la diméthicone, la glycérine, le kaolin, les dérivés de cellules de levures vivantes, la vaseline, l'huile de foie de requin, le bicarbonate de sodium, le soufre, l'acide tannique, la vaseline blanche, l'acétate de zinc, le carbonate de zinc et l'oxyde de zinc ainsi que leurs mélanges.

11. Procédé cosmétique de régulation de l'atrophie de la peau chez des mammifères, comprenant le traitement de la peau avec une quantité sans danger et efficace d'une composition comprenant:

(a) une quantité sans danger et efficace d'acide salicylique; et
(b) un véhicule hydro-alcoolique acceptable d'un point de vue pharmaceutique,

à l'exclusion des procédés de traitement du corps humain ou animal par chirurgie ou thérapie ou des méthodes de diagnostic.

12. Procédé selon la revendication 11, dans lequel la composition comprend de 0,01% à 50% d'acide salicylique, de préférence de 0,1% à 20% d'acide salicylique.

13. Procédé selon la revendication 12, dans lequel le véhicule acceptable d'un point de vue pharmaceutique est un véhicule à usage local, de préférence dans lequel le véhicule à usage local comprend:

(a) de 10 à 60 pour cent en poids de C_2H_5OH ou C_3H_7OH;
(b) de 30 à 80 pour cent en poids d'eau; et
(c) de 0,2 à 5,0 pour cent en poids de méthylalkyl(de coprah)taurate de sodium ou de méthyloléoyltaurate de sodium; la composition ayant un pH de 2 à 3,5.

14. Procédé selon la revendication 13, dans lequel le traitement de la peau avec la composition est un traitement chronique, ou dans lequel le traitement de la peau avec la composition s'effectue pendant une période d'au moins environ trois semaines comprenant l'application de la composition entre environ une fois par semaine et environ deux fois par jour.

15. Procédé selon la revendication 14, dans lequel la composition comprend en outre une quantité sans danger et efficace d'un écran solaire, de préférence dans lequel ledit écran solaire est choisi parmi le p-méthoxycinnamate de 2-éthylhexyle, le butylméthoxydibenzoylméthane, la 2-hydroxy-4-méthoxybenzophénone, l'acide octyldiméthyl-p-aminobenzoïque et leurs mélanges.

16. Procédé selon la revendication 14, dans lequel la composition comprend en outre, en une quantité sans danger et efficace, un autre agent actif choisi parmi un agent anti-inflammatoire, des vitamines, un antioxydant, un chélateur, un rétinoïde, un dérivé de benzofurane, un dérivé de N-acétyl-L-cystéine et un protecteur cutané, et leurs mélanges.

17. Procédé selon la revendication 15, dans lequel ledit agent anti-inflammatoire est choisi parmi l'hydrocortisone, l'hydroxyltriamcinolone, l'alpha-méthyldexaméthasone, le dexaméthasone-phosphate, le dipropionate de béclométhasone, le valérate de clobétasol, le désonide, la désoxyméthasone, l'acétate de désoxycorticostérone, la dexaméthasone, la dichlorisone, le diacétate de diflorasone, le valérate de diflucortolone, la fluadrénolone, le fluclorolone acétonide, la fludrocortisone, le pivalate de fluméthasone, le fluosinolone acétonide, le fluocinonide, l'ester butylique de flucortine, la fluocortolone, l'acétate de fluprednidène (fluprednylidène), la flurandrénolone, l'halcinonide, l'acétate d'hydrocortisone, le butyrate d'hydrocortisone, la méthylprednisolone, le triamcinolone acétonide, la cortisone, la cortodoxone, le flucétonide, la fludrocortisone, le diacétate de difluorosone, le fluradrénolone acétonide, la médrysone, l'amcinafel, l'amcinafide, la bétaméthasone et le restant de ses esters, la chloroprednisone, l'acétate de chlorprednisone, la clocortolone, la clescinolone, la dichlorisone, le difluprednate, le flucloronide, le flunisolide, la fluorométhalone, la flupérolone, la fluprednisolone, le valérate d'hydrocortisone, le cyclopentylpropionate d'hydrocortisone, l'hydrocortamate, la méprednisone, la paraméthasone, la prednisolone, la prednisone, le dipropionate de béclométhasone, la triamcinolone, le piroxicam, l'isoxicam, le ténoxicam, le sudoxicam, CP-14 304, l'aspirine, le disalcide, le bénorylate, le trilisate, la safapryne, la solprine, le diflunisal et le fendosal, le

diclofénac, le fenclofénac, l'indométacine, le sulindac, la tolmétine, l'isoxépac, le furofénac, le tiopinac, la zidométacine, l'acématacine, le fentiazac, le zomépiract, le clidanac, l'oxépinac et le felbinac, l'acide méfénamique, méclofénamique, flufénamique, niflumique et tolfénamique, l'ibuprofène, le naproxène, le bénoxaprofène, le flurbiprofène, le kétoprofène, le fénoprofène, le fenbufène, l'indoprofène, le pirprofène, le carprofène, l'oxaprozine, le pranoprofène, le miroprofène, le tioxaprofène, le surprofène, l'alminoprofène, et l'acide tiaprofénique, la phénylbutazone, l'oxyphenbutazone, la féprazone, l'azapropazone et la triméthazone ainsi que leurs mélanges.

18. Procédé selon la revendication 15, dans lequel ledit antioxydant ou piégeur de radicaux est choisi parmi l'acide ascorbique, le tocophérol, les acides hydroxybenzoïques butylés, l'acide 6-hydroxy-2,5,7,8-tétraméthylchroman-2-carboxylique, l'acide gallique, l'acide urique, l'acide sorbique, la N,N-diéthylhydroxylamine, l'aminoguanidine, les composés sulfhydryles et l'acide dihydroxyfumarique, leurs dérivés et leurs mélanges.

19. Procédé selon la revendication 15, dans lequel ledit rétinoïde est choisi parmi l'acide entièrement-trans-rétinoïque et l'acide 13-cis-rétinoïque et leurs mélanges.

20. Procédé selon la revendication 15, dans lequel ledit protecteur cutané est choisi parmi l'allantoïne, le gel d'hydroxyde d'aluminium, le sous-nitrate de bismuth, l'acide borique, la calamine, le beurre de cacao, l'amidon de maïs, la diméthicone, la glycérine, le kaolin, les dérivés de cellules de levures vivantes, la vaseline, l'huile de foie de requin, le bicarbonate de sodium, le soufre, l'acide tannique, la vaseline blanche, l'acétate de zinc, le carbonate de zinc et l'oxyde de zinc ainsi que leurs mélanges.